

DETERMINATION OF THE ATOMIC
REFRACTIVITY OF EPOXY-OXYGEN
EVIDENCE FROM HYDROCARBONS CONTAINING
TWO ISOLATED EPOXIDE RINGS

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PREFACE

A diepoxide is an organic compound in which there are two epoxy rings. According to the International Union of Chemistry (I.U.C.) and the Chemical Abstracts (C.A.) systems of nomenclature, the word "epoxy" is used to designate a ring of any size, consisting of one oxygen atom joined to two carbon atoms ultimately or directly joined to each other to form an otherwise isocyclic compound not so readily named in some other way. The compound below, for example, would be called 1,4-epoxynaphthalene according to each of the above systems:



In this dissertation, however, the term "epoxy" is limited to mean the ring formed when adjacent carbon atoms which are directly attached by a single bond are linked together through an oxygen atom. The epoxy ring is thus synonymous with the oxirane ring, $\begin{array}{c} \text{C} \quad \text{C} \\ \diagdown \quad \diagup \\ \text{O} \end{array}$.

Such terms as di-chlorohydrin, di-bromohydrin, and di-halohydrin are hyphenated to denote the existence of two separate halohydrin structures in the same molecule and to avoid the confusion introduced by an unhyphenated word like "dichlorohydrin," which may mean a chlorine atom on each side of, and adjacent to, a hydroxyl

group, as in glycerol dichlorohydrin, $\begin{array}{c} \text{CH}_2 - \text{CH} - \text{CH}_2 \\ | \quad | \quad | \\ \text{Cl} \quad \text{OH} \quad \text{Cl} \end{array}$

The common terms, "allylic" and "vinyllic" are used where they are essential to bring out differences of structure.

With respect to olefins and diolefins, however, the terminology and nomenclature used in this dissertation conform to the I.U.C. rules. Insertions of common names are made parenthetically because of their general acceptance. In those cases where structure has never been proved, the name originally assigned has been retained.

The atomic refractions used as a basis for calculation of the atomic refractivity of the epoxy-oxygen have been obtained from the revised data of both Eisenlohr and Vogel. In the case of very pure paraffins and cycloparaffins it has been found that Vogel's data gives slightly better results than Eisenlohr's. However, both are well within the limits of error introduced by (1) differences in polarization of the electrons in the various configurations of isomeric compounds, (2) errors in the determination of physical constants due to traces of impurities in the compounds, and (3) the temperature of the determination. (Increase in temperature usually causes increase in molar refraction.)

As is customary in research reports, all temperatures refer to the centigrade scale. Therefore, its symbol is omitted. Temperature readings have been made on thermometers standardized several times against sets of Anschütz thermometers calibrated by the Bureau of Standards. Unless otherwise indicated, temperature readings are at atmospheric pressure.

Fractionation pressures were determined by a Zimmerli gauge calibrated at 5.0 mm. Hg. against a modified McLeod gauge.

Inasmuch as the literature descriptions of syntheses of diepoxides are lacking in some essential points, the method of preparation of the diepoxides used in this investigation is given in detail.

The manner of listing references is the customary one for scientific reports. Journal abbreviations are as used in Chemical Abstracts.

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CHAPTER I

INTRODUCTION AND REVIEW OF THE LITERATURE

This research project was directed toward the determination of the atomic refractivity of oxygen specifically in the epoxy ring. Hitherto the value for oxygen in linear ethers has been used, because no greater loss of accuracy has resulted than occurs due to chain isomerism or to temperature of the determination of the density and refractive index, as mentioned in the Preface. However, since the epoxy ring has only three members, all bonds therein might be expected to be somewhat strained. Ring-strain is the only obvious reason for the much greater reactivity and lower stability of epoxides as compared to ethers. The normal bond-angle of oxygen in ethers is $100-110^\circ$,¹ whereas the corresponding angle in epoxyalkanes is $60-70^\circ$.¹⁻³ De Vries Robles⁴ has pointed out that the three atoms of the epoxy ring lie on the same plane, so it is unlikely that the angle formed by the carbon-oxygen and the carbon-carbon bonds is over 60° . Obviously, all the elements in the epoxy ring are joined by strained bonds. Refractive index depends upon the frequency of vibration of electrons, including those forming bonds, in a molecule which has been struck by light waves of a definite length. Therefore, differences in the degrees of constraint of the electrons forming corresponding bonds in epoxides and in ethers must be reflected by differences of bond refractions in epoxides and in ethers. Theoretically, the use of ether-oxygen atomic refraction (Eisenlohr, et al⁵⁻¹³) or ether carbon-oxygen bond refraction

(Vogel^{14,15}) for epoxy-oxygen atomic or bond refractions is erroneous.

The idea has long been entertained that the structure of organic molecules is indicated by some relationship of their physical constants, with each constituent of the molecule, whether atom or linkage, contributing a certain amount to the total value of the relationship shown by the molecule. Thus the relationship would be both additive and constitutive. Kopp¹⁶ first discovered two such relationships in terms of increase of boiling point and of molecular volume, M/d , resulting from insertion of a methylene group in a homologous series of compounds. Berthelot¹⁷ later showed that increase in boiling point is not constant even in a homologous series; therefore, it was not a good basis for estimation of structure. He made an extensive search for relationships, including boiling points, specific volumes and heats, heats of combustion, and a factor by which the molecular volume could be multiplied to give fair indications of the structure of compounds. His last relationship, molar refraction, was $R=(n^2-1)M/d$. The refractive indexes were determined in white light, which allowed an accuracy of 10^{-3} unit, although Deville¹⁸ previously observed that accuracy to the 10^{-4} unit demands use of light of specific wave lengths. Berthelot¹⁷ calculated the group refractivity of a methylene group with an average error of about 3 per cent. Later, Gladstone, *et al.*,¹⁹⁻²² Landolt,²³ and Wüllner²⁴ determined molar refractivities at a specific wave length, finally using the equation, $R_\lambda=(n_\lambda^2-1)M/d$. The average error in calculation of the group refractivity of a methylene group was 1.5 per cent. After Lorentz²⁵ and L. Lorenz²⁶ published their theoretical treatments of molar refraction, Landolt^{27,28} recalculated atomic

refractions based on the Lorens-Lorentz equation, $R_{\lambda} = \frac{n_{\lambda}^2 - 1}{n_{\lambda}^2 + 2} \frac{M}{d}$

which is still used. The theory of refractivity and its relationship to dielectric constants are given in every book on general physical chemistry; in addition there are several extensive treatises^{29,30} available, so the subject will not be discussed here.

The field of diepoxidation has been only cursorily explored, considering the length of time that diepoxidation has been known. Only about twelve diepoxides are known, and these have no relation to each other.

The first diepoxide, 1,2;3,4-diepoxybutane, was made by Przybytek³¹ in 1884 by the treatment of 1,4-dichloro-2,3-dihydroxybutane in ether with powdered potassium hydroxide. The existence of cis-trans isomerism in the diepoxyalkane series was proved by Griner (1893)³² when he dehydrohalogenated the bromohydrins obtained from the two isomeric 1,4-dibromo-2,3-butenes. Przybytek³³ closely followed his work on diepoxybutane with the preparation of 1,2;5,6-diepoxyhexane by dehydrohalogenation of 1,6-dichloro-2,5-dihydroxyhexane. He found, as did the writer, that the di-chlorohydrin could not be distilled without decomposition. Final purification of the diepoxide required hydration of the crude material almost to the epoxy-glycol, filtration of the aqueous solution from the chlorinaceous impurity, concentration, and slow vacuum dehydration in a desiccator back to the diepoxide. The yields of pure material were quite scanty, as would be expected. Bigot³⁴ (1891) obtained a compound closely akin to 1,2;5,6-diepoxyhexane by a Wurtz reaction, using epichlorohydrin and sodium.

Although his compound had an empirical formula of $C_6H_{10}O_2$, its specific gravity was too low and it boiled 25° below the true diepoxide reported by Przybytek.³³ The writer has prepared 1,2;5,6-diepoxyhexane which, although prepared by a different method, corresponds to that reported by Przybytek.³³ The structure of Bigot's compound is now being investigated.

Dehydrohalogenation was used also by Duden and Lams³⁵ to prepare 2,3;4,5-diepoxyhexane.

In 1909, however, a new method of epoxidation was published, one which circumvents formation of halogen compounds which later might contaminate the diepoxide. Prileshaev³⁶⁻³⁸ described the use of perbenzoic acid to epoxidize directly the unconjugated double bonds of terpenes. This method not only gives a purer product but also is much faster and more convenient. By it Prileshaev^{36,37} synthesized 1-methyl-1,2-epoxy-4-(1-methyl-1,2-epoxyethyl)cyclohexane [1-limonene diepoxide]. Lippmann³⁹ was actually the first to use perbenzoic acid, but his method did not give a smooth reaction and the yield of epoxide was low. Paul and Tchelitcheff⁴⁰ similarly obtained 1,2;4,5-diepoxy-pentane. Bauer and Bähr⁴¹ obtained the dioxide of 1,1'-dehydro di(cyclopentadiene-1,3) but failed with cyclopentadiene-1,3. Bedos and Ruyer⁴² prepared the dioxide of cyclohexadiene-1,3 in high yields. In the same year, 1932, Muscat and Herrman⁴³ prepared the dioxide of cis-phenylbutadiene-1,3.

Other organic peracids can also be used as epoxidizing agents. Karrer and Jucker⁴⁴ used perphthalic acid to diepoxidize β -carotene.

No mention was made of an attempt to saturate all the double bonds. Smit,⁴⁵ and Swern, et al.,^{46,47} have described the use of peracetic acid in anhydrous acetic acid to prepare epoxides of monoolefins, high molecular-weight fatty acids and vegetable oils. A diepoxide of 2-methyl-6-methylene-2,7-octadiene(myrcene) was obtained by treatment with peracetic acid in ether.⁴⁸ Arbuzov and Michailov⁴⁹ were able to duplicate the synthesis of levo-1-methyl-1,2-epoxy-4-(1-methyl-1,2-epoxyethyl)cyclohexane.

Alkaline hydrogen peroxide was used by Adams and Hers⁵⁰ to give the dioxide--possibly the diepoxide--of helenalin acetate.

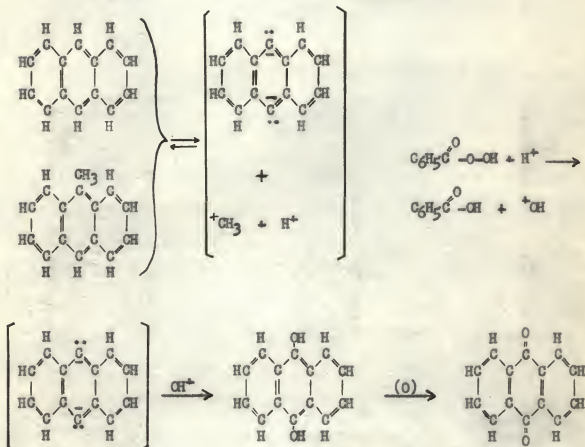
Diepoxides have also been obtained as by-products, in traces, from other reactions. Braun and Munch⁵¹ reported the isolation of very small amounts of 1,2;5,6-diepoxyhexane and 1,2;8,9-diepoxy-nonane from the acid-insoluble portions of the silver oxide decomposition products of 1,6-dihydroxy-2,5-di(1-piperidino) hexane and 1,9-dihydroxy-2,8-di(1-piperidino) nonane.

Monoepoxides have been obtained from the air-oxidation of olefins and from the dehydration of glycols. However, no examples of diepoxidation by one of these methods are to be found in the literature.

The normal course of oxidation of an olefin by an organic peracid yields an epoxide, a glycol, or a mono- or di-ester of the glycol. However, the literature contains many reports of such oxidations leading to the formation of other types of compound, such as aldehydes,⁵²⁻⁵⁷ ketones,⁵⁷ acids,⁵⁷ unsaturated alcohols,⁵⁴⁻⁵⁶ and heterocyclic derivatives.^{55,56,58,59}

Knowledge of the modern conception of how an organic peracid oxidizes an organic compound may prove interesting--

bond character as estimated by Pauling but on the carbon atoms nearest the axis of the aromatic skeleton. Both anthracene and 9-methylantracene, oxidized for six days at 0° , yielded anthraquinone. The mechanism which these investigators assumed is illustrated below:

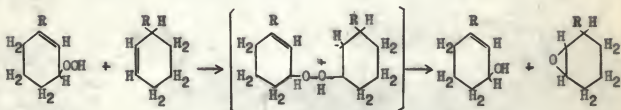
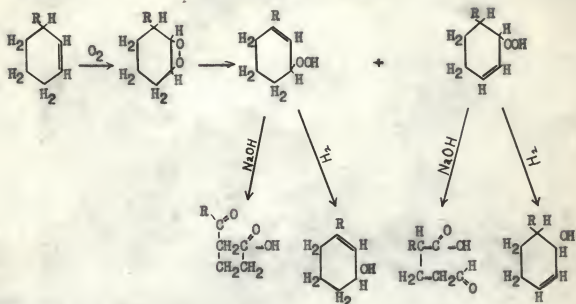


The substituents in the 9,10-positions of these hydrocarbons became hydrogen ions or charged methyl radicals. The hydrogen ions reacted with the peroxide oxygen (assumed by Swern⁶²) to become electrophilic hydroxyl groups. These electron-poor hydroxyl groups reacted with the electron-rich carbon atoms in the 9,10-positions, to form anthraquinol with both anthracene and its 9-methyl derivative. Anthraquinol is easily oxidized to anthraquinone by air. Some anthraquinone

may have been formed by the direct action of peroxide oxygen on the electron-rich 9,10-carbon atoms.

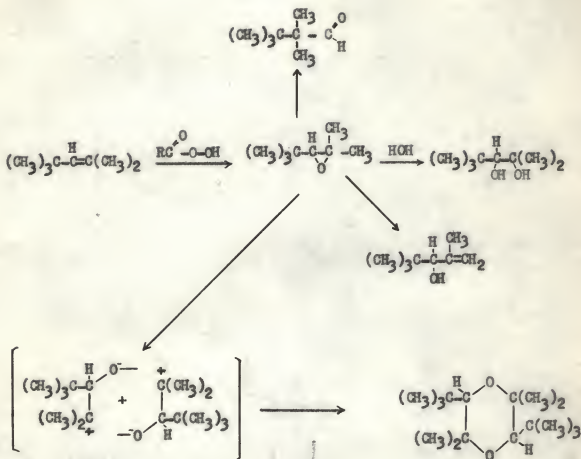
Hickinbottom and Byers^{54-56,64} treated 2,4,4-trimethylpentene-2 and 2,4,4-trimethylpentene-1 with peracetic acid and obtained a variety of products. On further study of the oxidation of 2,4,4-trimethylpentene-2 with various agents and reaction environments they isolated and identified compounds such as an allylic alcohol, 2,4,4-trimethyl-3-hydroxypentene-1; a cyclic diether, 2,2,5,5-tetramethyl-3,6-(1,1-dimethylethyl)-1,4-dioxane; and a small amount of an aldehyde, 2,2,3,3-tetramethylbutanal, in addition to the expected glycol, 2,4,4-trimethylpentanediol-2,3. The other octene derivative reacted analogously.⁵⁵ The formation of these unexpected compounds led Hickinbottom⁵⁴ to seek in the literature an oxidation system known to yield compounds of the types which were identified in his laboratory. The oxidation of olefins by molecular oxygen is known to cause the formation of epoxides, allylic alcohols, bimolecular oxygen compounds, and traces of carbonyl compounds. If oxidation by peracids is assumed to operate by a very similar mechanism to that by molecular oxygen, then peracids should yield compounds homologous to those cited above, and it may be argued that opening of the epoxide ring instead of the moloxide ring, $\begin{array}{c} \text{H} & \text{H} \\ | & | \\ -\text{C}- & -\text{C}- \\ | & | \\ \text{O} & \text{O} \end{array}$, or the formation and decomposition of hydroperoxides, might be the reason for the formation of the allylic alcohols, bimolecular oxygen compounds, and carbonyl compounds. The formation of the products obtained from the oxidation of an olefin by molecular oxygen according to the theory evolved by Hickinbottom's

references⁶⁴⁻⁷² can be represented as follows:



No decision on the explanation for the appearance of carbonyl compounds was found in the references, and Hickinbottom also failed to explain why 2,2,3,3-tetramethylbutanal was the carbonyl compound which was formed by the oxidation of 2,4,4-trimethylpentene-2.

Hickinbottom's theory⁵⁶ of the formation and subsequent reactions of 2,4,4-trimethyl-2,3-epoxypentane is illustrated in the following scheme of reactions:



Hickinbottom⁵⁴⁻⁵⁶ believes that the epoxide is the parent compound of all the products which he has obtained by oxidation of the trimethylpentenes with either peracetic or chromic acid. Considerable doubt has been expressed by various investigators⁷³⁻⁷⁹ that formation of the allylic alcohol and of the aldehyde, requiring migration of two alkyl groups and a hydrogen atom, proceeds from an epoxide intermediate under the reaction conditions employed for epoxidation. They^{73,75} seem to prefer to consider the glycol as the parent compound. This would be an interesting subject for extensive investigation.

CHAPTER II

SCOPE AND LIMITATIONS OF DIEPOXIDATION

Introduction

From the enumeration, in Chapter I (pp. 3-5), of the diepoxides which have been prepared, it is seen that comparatively few diepoxides have been made, although epoxidation is an old procedure and diolefins are commercially available. This may be even surprising, considering the utility of epoxidation as a tool in structural analysis^{50,80-82} and the wide use of epoxyethane both in the laboratory and in the plant.⁸³ The variety of compounds which can be made from epoxides should have excited the curiosity of investigators in the fields of pure organic chemistry and of fine chemicals such as dyes,^{84,85} perfumes,⁸⁵ pharmaceuticals,^{85,86} and detergents.⁸⁷

Possibly the fundamental reason that diepoxidation is not more common is that no coherent study of diepoxidation has ever been published. Therefore, an attempt will be made in this dissertation to describe the present status of various methods of diepoxidation.

Peracids

The use of organic peracids is generally accepted as the easiest way to prepare epoxides of monoolefins. Their use has been found essential for preparing diepoxides from hydrocarbons with isolated double bonds. The instability of organic peracids has proved

a great handicap in these syntheses since it has been necessary to prepare a fresh supply for each experiment. They have not been commercially available. Recently, however, a 40 per cent solution of peracetic acid in acetic acid was put on the market.* It is easier to prepare than perbenzoic acid, which still must be made in the laboratory as needed. Perbenzoic acid can readily be obtained dry and almost pure, while peracetic acid can be concentrated by vacuum distillation conveniently only to 88 per cent. Pure peracetic acid can be obtained by freezing and centrifuging of a concentrated solution a number of times. As Swern⁴⁷ has pointed out, it is an ideal reagent for large-scale reactions and might be employed in making diepoxidation a commercial process. Although a glacial acetic acid solvent reacts slowly with the epoxide ring at room temperature, lower temperatures make the rate of epoxidation impractically low in many cases. Therefore, glycol acetates are usually appreciable by-products from the epoxidation of olefins in acetic acid. This disadvantage can be eliminated largely by carrying out the epoxidation either by dissolving both reactants in a neutral dry organic solvent, such as ether or chloroform, using highly concentrated peracetic acid, or by dissolving the olefin in a small amount of the inert solvent and adding the concentrated peracid to it, utilizing the fact that peracid oxidations are bimolecular.⁸⁸ Both methods have been used; by either method only a small amount of decomposition product is obtained. The greater speed of oxidation⁴⁷ of a double bond by peracetic acid, compared to

*Buffalo Electro-Chemical Company, Inc. ("Becco"), Buffalo, New York

perbenzoic acid, also helps to keep the yield of epoxide appreciable when peracetic acid is used. If the sulfuric acid used to liberate perbenzoic acid is not thoroughly washed out of the organic solution of peracid and if a trace of moisture remains in the solution during reaction, hydrolysis and esterification of the epoxide formed occurs to yield a glycol monobenzoate.

Formation of glycols is the main cause of failure to obtain diepoxides with this type reagent. The effect of acids has already been mentioned. In the opinion of the writer, the major cause of hydration is the presence of an appreciable amount of water in the peracid solution due to inefficient drying. Sodium sulfate, the recommended drying agent for perbenzoic acid, is not satisfactory for drying solvents to be in contact with diepoxides later. At best, these derivatives are not very stable. Anhydrous calcium sulfate was added to a diolefin solution before reaction with perbenzoic acid in moist chloroform. Experiments indicate that its use is not advisable since it was found to destroy the perbenzoic acid. It is worth the time required to dry the solution by stirring with sodium sulfate, then to concentrate the peracetic acid solution or to distill as rapidly as possible all the chloroform from the perbenzoic acid preparation at 10-20 mm. Hg. pressure. The peracetic acid concentrate or the perbenzoic acid crystals are dissolved in dry ether and the solution standardized.* This procedure gives a peracid solution ready for oxidations.

*Ether seems better than chloroform as a reaction medium.

It has been reported that olefins having alkyl groups in the vinyl position are very quickly oxidized,⁸⁸⁻⁹¹ but a positive diepoxide was not obtained from 2,5-dimethylhexadiene-1,5 after standing in a chloroform solution of perbenzoic acid for two days at room temperature. The presence of an aryl group in the molecule reduces the speed of oxidation.⁹⁰ Conjugation of a double bond with another double bond results in marked resistance to oxidation.^{36,37,92-96}

The only statements of the limitations of methods of diepoxidation were made by Prilezhaev³⁶ and by Swern.⁴⁷ Only Swern's statement—the usual solvent, glacial acetic acid, for peracetic acid opens the epoxide ring at the rate of about one per cent per hour at 25°, yielding hydroxy acetoxy compounds—has not required modification in the light of later work. Prilezhaev³⁶ stated that perbenzoic acid and possibly other peroxides are useless for the epoxidation of diolefins with conjugated double bonds. Reindel⁹⁵ and then Pummerer and Reindel⁹⁶ published work in complete agreement with the above statement. They could oxidize butadiene-1,3 and 2-methylbutadiene-1,3 to the monoxides by using perbenzoic acid in ethyl chloride. Later, however, five exceptions to the statement about non-reactivity of peracids with conjugated double bonds were published. Bauer and Bahr⁴¹ found that both cyclopentadiene-1,3 and 1,1'-dehydrodi(cyclopentadiene-1,3) react with perbenzoic acid in more than molar ratios, and isolated 1,1'-dehydrodi(cyclopentadiene-1,3) dioxide. Smit⁹⁷ determined from the rate of disappearance of peracetic acid during its action upon fatty acids having conjugated and unconjugated double bonds that oxidation did not stop abruptly after the first double bond in the conjugated acid had

been epoxidized, but that the reaction was only greatly slowed down. Karrer and Jucker⁴⁴ isolated a diepoxide of the conjugated decaolefin, β -carotene. The diepoxides of 1,3-cyclohexadiene⁴² and cis-phenyl-butadiene⁴³ have also been prepared.

However, Prilezhaev's statement about conjugated double bonds remains essentially true. In his own^{36,37} work and in that of other investigators,⁹²⁻⁹⁶ it has been found that a double bond conjugated with a carbonyl or carboxyl group, as well as with another carbon-to-carbon double bond, is resistant to oxidation.

Prilezhaev's work in the field of terpene chemistry was indeed so outstanding that perbenzoic acid is commonly used in this field. A short discussion of its uses therein serves to illustrate another limitation of peracids.

Prilezhaev himself^{36-38,80} used the chemical almost entirely to identify terpenes by epoxidation. However, by his method of oxidation, certain terpenes absorbed oxygen from the peracid quantitatively. This led Nametkin and Bryusova⁸¹ to use the acid to distinguish between double bonds, which absorb oxygen, and trimethylene rings, which do not. Furthermore, they estimated the proportion of unsaturated terpenes in impure samples. Ruzicka, *et al.*,⁸² similarly determined the number of double bonds in α - and β -amyrins and their derivatives. These determinations are based, of course, upon the number of active oxygen atoms absorbed by a unit weight of terpene in the presence of excess perbenzoic acid. The excess active oxygen is determined iodometrically. However, Meerwein, *et al.*,⁹⁸ pointed out that compounds of the type $R_2C=CH_2$, for example camphene and α -

fenchene, and benzalacetone absorb more than one atom of active oxygen per double bond over a period of several days, introducing a serious error. He suggested the use of rate of oxidation to differentiate among various terpenes. It was found later by Böeseken, *et al.*,⁹⁹⁻¹⁰¹ that perbenzoic or peracid acid reacts with benzalacetone to give 2-phenyletheryl acetate. Recently Friess¹⁰² reported that perbenzoic acid oxidizes some simple ketones to esters. The reaction may be illustrated as follows, where $R' > R$:



As would be expected, peracids may react with triple bonds,^{103,104} but compounds having a structure, $-C \equiv C-$, probably do not exist in nature.

Yet, despite the fact that peracids react only very slowly with a double bond conjugated with another double bond but do react with compounds having apparently no oxidisable structure, perbenzoic acid is still used occasionally to estimate unsaturation in carotinoids⁸² and plastics.¹⁰⁵

Dehydrohalogenation of Halohydrins

The preparation of epoxides by treatment of an olefin by aqueous hypochlorous acid solution, followed by dehydrohalogenation with caustic, has been the usual laboratory method. Certainly not so many epoxides have been prepared by other methods, such as dehydration of glycols, treatment of olefins by peracids, or direct catalytic oxidation of olefins by oxygen or air. The last method is used

commercially for the preparation of epoxyethane.⁸³

In the preparation of diepoxides, however, halogenation can be either an extremely poor method or the only practical one. For the preparation of diepoxides from diolefins containing isolated double bonds, the method is definitely not recommended because of the difficulty of preparing the di-chlorohydrin in good yield and of maintaining pressures sufficiently low for its efficient fractionation. The author was unable to distill the di-chlorohydrins either of hexadiene-1,5 or of isomeric methylpentadienes at 0.5 mm. Hg without extensive decomposition. The development of molecular stills, particularly of the falling film type made entirely of glass, may allow purification. Diepoxides made by way of di-halohydrins were usually produced by adding caustic either to the residue left after distillation of the ether extractant, as in the case of the diepoxidation of hexadiene-1,5 or to solid di-halohydrins such as 2,5-dibromohexanediol-3,4 or 1,4-dichloro-2,3-dihydroxybutane.

Di-halohydrins of diolefins containing conjugated double bonds seem to be solids, on the basis of the halohydrins of butadiene-1,3 and hexadiene-2,4; since they are capable of being recrystallized, high-vacuum fractionations are not required. This is indeed fortunate because diepoxidation by way of di-halohydrins is the only general method available for conjugated diolefins. Its value is based upon the addition of halogens in the 1,4-positions of conjugated double bonds in the cold, which causes formation of a double bond in the 2,3-position. This double bond can be hydrated to a glycol by mild oxidation, yielding a 1,4-dihalo-2,3-dihydroxy compound.

This method is limited by the difficulties of purifying liquid di-halohydrins and of separating traces of halides from the diepoxide, the final product. Substituents on the carbon atoms in the 2- or the 3- position cause, upon oxidation, formation of tertiary alcohols. These alcohols are very sensitive to heat or strong alkalis. Substitution by this method in the 1- or the 4- position should facilitate diepoxidation. Yields are not high at any stage of the process. Di-halohydrins containing alkali-sensitive structure not supposed to be removed; such as aldehydes, esters, nitriles, bromides, or iodides; cannot be diepoxidized.

However, the method is applicable to most commercially available diolefins since they contain systems of conjugated double bonds. Furthermore, pure conjugated diolefins can be produced with less difficulty and expense than those with isolated double bonds. Improvements in methods of agitation and rectification should increase the yields of intermediates and of diepoxides. The problems involved in the production of any conjugated diepoxide found commercially useful are challenging but should not be insuperable.

Other Methods

Reports of the isolation of diepoxides by other methods have been cited in Chapter I, pp. 3-5, but the methods described do not appear promising.

Braun and Münch⁵¹ isolated very small quantities of impure diepoxides as by-products of the decomposition of diamines.

Adams and Herz⁵⁰ used alkaline hydrogen peroxide to diepoxidize acetylhelenalin, a ketotriolefin having one unconjugated double bond. Hydrogen peroxide is a more powerful oxidizing agent than peracids, but the yields of diepoxide are rather low and the method is not trustworthy. The oxidizing power of this reagent may also affect other parts of the molecule, such as labile hydrogen atoms.

The dehydration of tetrahydroxy glycols would probably lead to unsaturated alcohols, cracking, etherification or polymerization. Even if diepoxides were formed, they would be likely to form oxygenated rings such as furan derivatives.

Direct catalytic oxidation of diolefins is a process that may be found workable. This method would involve passing oxygen or air mixed with diolefin vapor over beds of catalyst, removing the oxidized product as it is condensed, and recovering or recycling the unreacted material. The expense of the research to determine optimum reaction conditions could be justified only by a large, ready market for the products obtained.

CHAPTER III

EXPERIMENTAL WORK

Preparation of Intermediates

Peracetic acid is commercially available. Perbenzoic acid, however, is not on the market and therefore must be made whenever needed.

Perbenzoic acid has been prepared by nine methods: (1) by acidulation of sodium perbenzoate formed from sodium ethoxide¹⁰⁶⁻¹⁰⁸ or methoxide¹⁰⁹ and benzoyl peroxide; (2) from benzoyl chloride and sodium peroxide;¹¹⁰⁻¹¹² (3) from benzoic acid and hydrogen peroxide;¹¹³ (4) from an acetone solution of benzaldehyde and acetic anhydride in an atmosphere of oxygen;¹¹⁴⁻¹¹⁶ (5) by the action of ultraviolet radiation on benzaldehyde;¹¹⁷ (6) by treatment of benzaldehyde with oxygen-ozone mixtures;¹¹⁸⁻¹²⁷ (7) by the reaction of benzoic acid with ozone;¹²⁰ (8) by hydrolysis of benzoyl acetyl peroxide with sodium ethoxide;^{128,129} and (9) by the treatment of benzoic anhydride with alkaline aqueous solutions of persalts or hydrogen peroxide.^{128,130-133}

The method of Braun¹⁰⁹ was used, obtaining the peracid by the action of sodium methoxide in anhydrous methanol upon benzoyl peroxide¹³⁴ in dry chloroform followed by acidulation with dilute sulfuric acid and extraction. Commercial methanol was dried by stirring for an hour with flake caustic to remove impurities, such as formaldehyde, and most of the water, followed by refluxing over magnesium turnings for a

few hours before distillation. The chloroform was dried by stirring with flake caustic to remove the hydrogen chloride formed by dry chloroform on standing, and was distilled. The purification of solvents is not stressed in the description of the procedure used, but it has been found to influence yields greatly. The procedure was modified by use of dry ice and acetone instead of an ice-salt mixture to cool the solution during the addition of the benzoyl peroxide and throughout the reaction. These modifications were designed to avoid a long period of addition of benzoyl peroxide solution, since an extended addition period complicates temperature control.

Chloroform was usually used to extract the peracid from aqueous solution before diepoxidation. However, since low yields of diepoxides in this project are attributed to insufficient drying of the solution and since sodium sulfate, an inefficient drying agent, is the only one recommended for drying solutions of perbenzoic acid, it is considered wise to isolate the dry acid by solvent evaporation and to transfer it to an anhydrous solvent before using it as an oxidizing agent. The products involved obviate the use of ether for the extraction although a very low-boiling solvent would be desirable.

Commercial sodium methoxide has been found very inferior to that made in the laboratory by dissolving sodium metal in methanol.

The major difficulties in this project have been encountered in the preparation of the diolefins rather than in the synthesis of the diepoxides. Powerful stirring motors, rigid stirrers, a supply of large strong flasks, and efficient fractionation apparatus, requisite

for maximum performance in such a project, have not been available, since they are not usually feasible in the collegiate organic research laboratory.

Double bonds occur in almost all of the few commercially available diolefins. Diolefins with isolated double bonds are usually made by a Wurts reaction, using one or more haloolefins in ether suitable for Grignard reactions. The haloolefins used in this project either are commercially available, such as allyl and methallyl chlorides, or were made more or less easily. Among those prepared were 1-chlorobutene-3 and isomeric crotyl chlorides.

Isomeric crotyl chlorides were made by reduction of dried redistilled technical grade crotonaldehyde according to the procedure of Nystrom and Brown.¹³⁵ The alcohol was chlorinated by the technique of Charon.^{136,137} Attempts to prepare the chloride from butadiene and dry hydrogen chloride in glacial acetic acid by the direct method of Kharasch, Kritchewsky, and Mayo¹³⁸ failed because a heavy glass tube could not be made with a closure strong enough to withstand the gas pressure existing before reaction. It was considered dangerous to seal the neck of the tube with a flame. Reduction of crotonaldehyde by aluminum isopropylate^{139,140} gave low yields of alcohol, probably because of impurities in the reducing agent. Aluminum isopropylate can now be purchased.*

The preparation of 1-chlorobutene-3 is difficult without the heavy reaction equipment mentioned above. Juvala¹⁴¹ found that the

*Tennessee Eastman Corporation, Kingsport, Tennessee

best yield of 1-butenol-4 was obtained when one mole of allyl bromide in 90 ml. of anhydrous ether was added to one mole of fine, dried magnesium turnings. Sufficient allyl bromide was not available, so the bromide was used only as a starter; the chloride was used during the remainder of the reaction. The use of twice as much ether as directed was necessary to make the reaction mass at all workable. The yield of alcohol was about 25 per cent. (Juvala¹⁴¹ reported 26 per cent.)

The diolefins were prepared by modifications of the procedure described by Henne and Chanan¹⁴² and by Henne, Chanan, and Turk.¹⁴³ The method used in this laboratory was: A solution of about seven moles of pure, dry, mixed chlorides of the allyl structure dissolved in 2500 ml. of pure, dry diethyl ether was added to four moles of magnesium turnings covered by 200 ml. of ether in a three-liter three-necked flask equipped with a self-vented addition funnel, both of which had been previously flamed to desorb moisture on their walls. The flask was provided with a mercury-sealed, rigid stirrer equipped with a stainless steel continuous arc blade curved to fit the bottom of the flask, and an efficient, high-capacity condenser cooled with ice water. Since an extremely rigid stirrer attachment was required, the shaft of the stirrer was screwed directly into the drive-shaft of a low-speed, high-torque one-eighth horsepower motor. Additional speed control was supplied by a transformer. This equipment is also required for the preparation of 1-butenol-4.

The allylic chlorides solution was added as fast as the condenser capacity allowed. Stirring was continued overnight, when

possible; otherwise, incompletely reacted magnesium was scraped down into the reaction zone and the mixture was allowed to stand overnight with tap-water running through the condenser. The use of a large bath of hot oil is dangerous. It would be better to use a commercial mantle having a pyrometer. The flask was then heated gradually in an oil-bath to 250° . The distillate was collected in a receiver cooled by an ice-salt mixture to minimize the loss of diolefins, since even those which boil above 100° are quite volatile. This procedure allows recovery of Grignard ether and obviates the need for drying agents. Such small amounts of reactants usually remain that retreatment with magnesium is not necessary and the distillate can be fractionated immediately over sodium. A fractionating column as efficient as possible should be used because members of diolefin mixtures are not easy to isolate. When fairly pure and thoroughly dry allylic chlorides are used, the weight of mixed diolefins obtained from a synthesis carried out as described above is at least 50 per cent theoretical.

The preparation of di-halohydrins was attempted numerous times in order to duplicate the methods of syntheses described in the literature and to prepare a diepoxide from a commercially available diolefin.

All attempts to duplicate Przybytek's synthesis³³ of 1,6-dichloro-2,5-dihydroxyhexane by direct hypochlorination of 1,5-hexadiene failed. A purple or a brown oil resulted from treatment of the diolefin with hypochlorous acid prepared by the method described in Organic Syntheses, 2nd ed., Coll. Vol. I, p. 158(1945). As would be expected, the oil could not be purified either by distillation at

0.5 mm. Hg pressure or by steam distillation. Even superheated steam was ineffective. Treatment of the crude di-chlorohydrin remaining after distillation of the ether extracted with powdered potassium hydroxide followed by fractionation at atmospheric pressure, as was described in the original article, gave thermal-decomposition products only. Similar failures resulted from efforts to synthesize the di-chlorohydrins of commercially available isomeric methylpentadienes. A batch of the ether extract was filtered and distilled; the residue would not freeze in an acetone-dry ice bath. A similar residue decomposed upon distillation at 0.5 mm. Hg pressure.

A more complicated, indirect method has been published by Detoeuf.^{144,145} His method, involving the preparation of, and hypochlorination with, N-chlorocarbamide (monochlorourea), gives excellent results and is now widely used in France. This method of synthesis was not attempted in this study.

The stepwise preparation of the di-bromohydrins of isomeric methylpentadienes by way of 1,4-addition of bromine¹⁴⁶ followed by mild oxidation to a glycol³⁵ was attempted several times. The dibromomethylpentenes, b₁₃ 76.5-78.5°, were obtained in reasonable yield, about 40 per cent, but oxidation of the olefin to a glycol, using 5 per cent aqueous potassium permanganate solution was unsatisfactory. The heavy precipitate of manganese dioxide by-product was removed from the oxidized dibromomethylpentene in aqueous alcohol by suction filtration through coarse paper. The filtrate was clarified and decolorized by addition of a small amount of dilute sulfuric acid and sodium

bisulfite, then was concentrated in vacuo to half its volume. A temperature below 35° during the concentration is preferable. The concentrate was saturated with sodium chloride and extracted with ether. The ethereal extracts, however, did not contain much oxidized dibromopentene; and the latter product, a yellow-brown, mobile fluid, decomposed upon distillation at 5 mm. Hg. No attempt was made to isolate the dibromoglycol by crystallization in a freezing mixture.

Reconsideration of the experimental results suggests that concentration of the filtrate from the reaction should have been continued to a small volume at temperatures below 35° , until the start of precipitation of inorganic salts. Then extraction of the concentrate with equal volumes of ether would remove almost all of the glycol from its aqueous solution. Thorough drying of the extracts and vacuum evaporation of the solvent at or below room temperature should yield the crude dibromoglycol containing a little solvent. The concentrate might then be solidified, in a freezing-mixture if necessary, and finally recrystallized. There is a strong possibility that one of the hydroxyl groups in the dibromoglycol is tertiary; a tertiary hydroxyl group would decrease the resistance of the compound to the heat level necessary for its isolation and purification. It will be noted that the di-bromohydrin prepared by Duden and Lemme,³⁵ 2,5-dibromo-3,4-dihydroxyhexane, does not contain a tertiary hydroxyl group. A further investigation of this method of preparing diepoxides should prove instructive. The writer has prepared several unsaturated alcohols suitable for conversion into conjugated diolefins and, in

addition, a few pure diolefins are commercially available; therefore, the feasibility of the method can soon be ascertained.

Preparation of Diepoxides

General Procedure of Diepoxidation

No method for the formation of diepoxides from di-halohydrins can be described from the experience of the writer because of his failure to obtain reasonably pure di-halohydrins. Procedures of dehydrohalogenation of mono-halohydrins described in the literature must be consulted for details.

The use of peracids for direct conversion of diolefins containing isolated double bonds into diepoxides has been the main subject of investigation in this laboratory. Swern⁶¹ has written an excellent review of peracids and their uses for oxidation of monoolefins. However, considering the brevity of details of experimental methods for epoxidation of diolefins by peracids, as mentioned in the literature, the writer is describing at length the method of synthesis which he has evolved in the course of preparing the diepoxides obtained in this project. Modifications of procedure can be made easily in order to raise the yield of any particular diepoxide synthesized.

The diolefin is dissolved in anhydrous chloroform in a three-necked, round-bottomed flask equipped with a fast mechanical stirrer, a dropping funnel, and a low-temperature thermometer. The solution in the flask is cooled by an acetone-dry ice bath to a temperature of

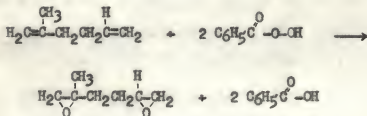
about -20° initially. The peracid solution, which has been cooled in an acetone-dry ice bath to -25° , is added in a thin stream during vigorous stirring. The temperature of the solution at the end of the addition period should not be greater than -10° . This precaution obviates the need for a long period of addition and minimizes the sensitivity of the reactants to local excesses of reagent. When the addition is over, the cooling bath is removed. Stirring is continued until the temperature of the solution rises above that of the room and then returns to room temperature. The reaction temperature has never risen above 40° (in a solvent of chloroform), but it is advisable to cool the flask if its contents reach temperatures much higher than 30° . The solution is then stored at room temperature until determination of excess active oxygen indicates that the reaction is at least 90 per cent complete. Accurate determinations of excess oxygen are possible only if spontaneous decomposition in the solution is avoided. The addition of 10 per cent benzene usually will prevent spontaneous decomposition of the peracid in chloroform. The reaction requires three to seven days in chloroform. (Anhydrous ether is the preferred solvent according to the literature, but great difficulty has been experienced in obtaining reasonable yields of perbenzoic acid upon removal of chloroform.)

The chloroform is then treated as follows: Any residual desiccant is separated and any of the acids present are removed by extraction with a mixture of ice and 5 N sodium hydroxide solution. For extra protection of the diepoxides, the solution is then washed with

dilute carbonic acid until the washings become acidic. At least two washings are required in order to ensure complete removal of perbenzoic and benzoic acids. The solution is then dried over sodium sulfate and distilled on a steam bath. The residue is filtered through dense paper, and the last traces of solvent are removed by aspiration on the steam bath. The residue is finally rectified in vacuo through a short Vigreux column, using an oil bath as the source of heat. A colorless, rather viscous liquid is obtained, smelling like perfume. The attainment of reasonably high purity requires at least three rectifications. Diepoxides not only are corrosive to stainless steel, the usual packing of the more efficient fractionating columns, but also are not generally very stable toward heat. The use of columns much more efficient than the Vigreux type is therefore disadvantageous. It is advisable to store diepoxides in a refrigerator because of their reactivity and low thermal stability.

Preparation of New Compounds

(A) Synthesis of 2-Methyl-1,2;5,6-diepoxyhexane:



A freshly prepared solution of 0.720 moles perbenzoic acid in 1500 ml. chloroform, dried one hour by stirring with anhydrous sodium

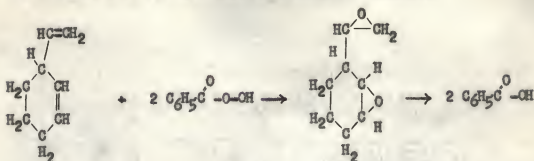
sulfate, was added to 43.5 gm. (0.340 moles) of 2-methylhexadiene-1,5 in 155 ml. dry chloroform within an hour. The reaction was carried out as described in the preceding section. Stirring was continued for four hours after the end of the addition of peracid, corresponding to three hours after the maximum reaction temperature of 37° had been reached. The solution was allowed to stand at room temperature. At the end of eighty-five hours, iodometric titration showed that the reaction was 100 per cent complete and autodecomposition of the peracid had begun. The solution was worked up as described in the preceding section.

After five rectifications, the diepoxide showed no further purification. The yield was 11.2 gm., corresponding to 25.7 per cent of the theoretical amount, based upon the 2-methylhexadiene-1,5 used.

The following physical constants and analytical data were determined for this compound:

B.p.	70.0-71.0°/10 mm.
n_D^{25}	1.4393
D_4^{25}	0.9958 gm./mole
M_p	33.873
C, %	Theoretical, 65.59; found, 65.52
H, %	Theoretical, 9.44; found, 9.50
Epoxy-O, % ¹⁴⁷	Theoretical, 24.97; found, 25.33

(B) Synthesis of 1,2-Epoxy-3-(epoxyethyl)cyclohexane:



A freshly prepared solution of 0.488 moles perbenzoic acid in 1500 ml. chloroform, dried one hour by stirring with sodium sulfate, was added to 25.0 gm. (0.2315 moles) 3-ethenylcyclohexene-1 in 75 ml. dry chloroform within an hour. The reaction was carried out as described in the preceding section. The maximum temperature of the solution was not determined.

The reaction was complete within forty-eight hours standing at room temperature. The solution was worked up as described previously. The oil obtained is a slightly viscous, sweet-smelling liquid soluble in organic solvents. The yield was 15.0 gm., corresponding to 10.7 per cent of theoretical, based upon the 3-ethenylcyclohexene-1 used.

The following physical constants and analytical data were determined for this compound:

B.p.	92.0-93.0°/5 mm.
$n_D^{27.0}$	1.4753
$D_4^{27.0}$	1.0876 gm./mole
M_{TP}	36.305
C, %	Theoretical, 68.56; found, 68.14
H, %	Theoretical, 8.63; found, 8.83
Epoxy-, % ¹⁴⁷	Theoretical, 22.82; found, 21.64

Determination of Atomic Refractivity

Inasmuch as this research project has been directed toward the determination of the atomic refractivity of epoxy-oxygen, greater care had to be taken in determination of molar refractivity than is usually required.

The diepoxides were purified as thoroughly as possible by rectification in vacuo. The index of refractions were determined on an ordinary Abbé refractometer which had been calibrated against toluene; 2,2,4-trimethylpentane; and methylcyclohexane, the refractive indices of which have been certified by the National Bureau of Standards. The densities were determined by enclosing in a vented moisture-tight container an unstoppered density bottle filled with the sample. The container and density bottle were kept immersed in the bath which supplies water of constant temperature to the refractometer prisms. The temperature of the bath was 0.3° lower than that of the prisms, but the time of transfer of the density bottle and contents from the bath to the balance, where the bottle was stoppered, wiped off, and weighed, was calculated to allow a temperature rise of $0.2-0.4^{\circ}$. The density bottle has a capacity of 5 ml. and was weighed to four significant figures.

The molar refractivities were determined on a calculating machine to only four significant figures because of uncertainty in the density determination. The maximum absolute error introduced by this

degree of uncertainty is only 0.005 ml., according to the equation,

$$\nabla R_{\text{max.}} = R \left[\frac{6n}{(n^2 - 1)(n^2 + 2)} \nabla n + \frac{\nabla d}{d} \right], \text{ where}$$

∇ is degree of error,

R is molar refraction,

n is refractive index, and

d is density.

Fajans¹⁴⁸ recommends that "in computing molar refractions the experimental values of the nearest homologous substances be used whenever possible." This advice has been followed approximately by subtracting from the molar refractivities of the diepoxides the molar refractivities experimentally determined on the corresponding saturated hydrocarbons minus the calculated values, 4.400, of the four replaced hydrogen atoms. The differences between the molar refractivities, divided by two, represent the atomic refractivity of each epoxy-oxygen.

This procedure yielded a variation of only 0.03 ml. out of 1.85 ml. (98 per cent precision).

TABLE I

REFRACTIVITY OF EPOXY-OXYGEN

Compound	Molecular Weight	Density	Refractive Index	Molar Refraction		Atomic Refractivity of Epoxy-Oxygen	Bond Refractivity of Epoxy-Oxygen
				Diepoxide	Parent Hydrocarbon		
1,2;4,5-diepoxypentane	100.11	1.071 ₂₀	1.436 ₂₀	24.42	25.37 ¹¹ ₁₉	1.78	1.44
1,2;5,6-diepoxhexane ^a	114.14	1.027 _{26.6}	1.439 _{26.6}	29.226	29.928 ¹⁵ ₀	1.85	1.50
2-methyl-1,2;5,6-diepoxhexane	128.17	0.995 _{8.25.0}	1.439 _{25.0}	33.873	34.526 ¹⁵ ₁	1.87	1.51
3-(epoxyethyl)-1,2-epoxycyclohexane	140.18	1.087 _{6.27.0}	1.475 _{27.0}	36.305	37.032	1.84	1.49

^aReported by Praybylek³³ and Braun and Münch⁵¹ but no data except b.p. given.

SUMMARY

This research project has yielded the following results:

(1) The atomic refractivity of epoxy-oxygen has been found to be 1.85 at 27°, using the D-lines of sodium. Their value is in good agreement with that of Flores-Gallardo and Pollard.¹⁵³

(2) Two new diepoxides, 2-methyl-1,2;5,6-diepoxyhexane and 1,2-epoxy-4-epoxyethylcyclohexane, have been prepared and their physical constants, as well as those of 1,2;5,6-diepoxyhexane, have been determined.

(3) An analysis of methods of diepoxidation has been given, and a general method of epoxidation of diolefins with isolated double bonds by the use of perbenzoic acid has been described in detail.

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BIOGRAPHICAL ITEMS

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This dissertation was prepared under the direction of the Chairman of the candidate's Supervisory Committee and has been approved by all members of the Committee. It was submitted to the Graduate Council and was approved as partial fulfilment of the requirements for the degree of Doctor of Philosophy

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